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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/073,300	02/13/2002	Yoram Reiter	02/23339	6257

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EXAMINER	
VANDERVEGT, FRANCOIS P	

ART UNIT	PAPER NUMBER
1644	

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DATE MAILED: 03/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/073,300	REITER, YORAM	
	Examiner	Art Unit	
	F. Pierre VanderVegt	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 4-13* is/are pending in the application.

4a) Of the above claim(s) *4-11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,12 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application is a continuation-in-part of U.S. Application Serial Number 09/534,966.

Claim 3 has been canceled.

New claims 12 and 13 have been added.

Claims 1, 2 and 4-13 are currently pending.

Election/Restrictions

1. **Claims 4-11 stand withdrawn** from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on June 8, 2004.

Accordingly, **claims 1, 2, 12 and 13 are the subject of examination** in the present Office Action.

2. **In view of Applicant's amendment filed September 8, 2005, the following ground of rejection has been maintained.**

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 1 and 2 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Mottez et al (J. Exp. Med. [1995] 181:493-502; U on form PTO-892, of record) in view of Lone et al (J. Immunotherapy [1998] 21(4):283-294; V on form PTO-892, newly cited).

It was previously stated: "Mottez teaches single chain constructs comprising a murine MHC class I heavy chain joined to β_2-microglobulin with a covalently bound antigenic peptide. Mottez teaches that linker, or spacer, sequences separate the segments (see entire document).

Mottez does not specifically teach human MHC class I heavy chain or β_2-microglobulin. However, in a continuation of the same work, Lone teaches that the same techniques were applied to human MHC class I heavy chain HLA-A2.1, which was joined via a 15-amino-acid linker to human β_2-microglobulin. Lone teaches that the single chain MHC class I construct folded properly and was functional (Abstract in particular). Lone teaches that the single chain MHC class I construct specifically

bound HLA-A2 restricted peptides and induced peptide-specific cytotoxic T cells to proliferate and produce IL-2.

It would have been prima facie obvious to a person having ordinary skill in the art at the time the invention was made to substitute human MHC class I as taught by Lone for the murine MHC class I bound to a specific peptide as taught by Mottez. One would have been motivated, with a reasonable expectation of success by the showing of Lone that the human MHC class I complex associated with peptide and activated T cells as well as the murine MHC class I complex did. One would have been further motivated by the teaching of Mottez that single chain MHC class I complexes can be useful for manipulating an immune response, particularly to an antigen that has low affinity for the MHC molecule (page 501, 2nd column in particular)."

Applicant's arguments filed September 8, 2005 have been fully considered but they are not persuasive.

Applicant argues that the prior art does not render the claimed invention obvious because the MHC class I complexes taught by Mottez and Lone are derived from eukaryotic cells. Applicant argues therefore that peptides must first be stripped from the single chain MHC class I molecules so that the MHC class I can be loaded with the peptide of interest. Applicant further argues that this stripping process is inherently incomplete and some of the endogenous peptide is left associated with at least a portion of the MHC class I complexes. Applicant concludes that Mottez/Lone does not teach the invention as claimed following amendment because the MHC class I complexes of Mottez/Lone cannot all bind to a single specific CTL clone. However, new matter issues not withstanding, Applicant is arguing limitations that are not in the claims. The claims are drawn to a "composition," which is a mixture of components, "comprising," which is open language meaning it contains, a "plurality of complexes [...] recognizable by a single specific CTL clone." The composition is not entirely made of the recited "plurality of complexes," but rather "comprises" the plurality. The language of the claim does not exclude the presence of MHC class I complexes that present peptide to other specific CTL clones, so long as it comprises a plurality of complexes that are recognizable by a single specific CTL clone. Based upon the evidence that the complexes taught by Mottez/Lone are capable of stimulating a clonal population of CTL, it is clear that the composition of Mottez/Lone comprises the required plurality. Accordingly, the ground of rejection is maintained.

4. **In view of Applicant's amendment filed September 8, 2005, the following NEW GROUNDS of rejection have been necessitated.**

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1, 2, 12 and 13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

Claim 1 has been amended by Applicant in a flaming attempt to differentiate the claimed invention from the prior art. Applicant asserts that support for the amendments to the claims can be found in the original claims and throughout the specification.

Claim 1 has been amended to recite, and new claim 13 recites, "biologically functional β_2M" and "biologically functional human MHC class I heavy chain." However, review of the specification and claims as originally filed shows numerous recitations of "functional β_2M" and "functional human MHC class I heavy chain," but no recitation of "biologically functional." The term "biologically functional" is not even defined in the specification in general terms. The specification defines the term "functional" at page 22, lines 3-8 as being:

> "As used herein the term "functional" when used in reference to the B-2 microglobulin and heavy chain polypeptides regions of a single chain MHC class I complex refers to any portion of each which is capable of contributing to the assembly of a functional single chain MHC class I complex (i.e., capable of binding and presenting to CTLs specific antigenic peptides when complexed)."

The definition does not address the term "biologically functional." While *ipso facto* support in the specification or claims as originally filed is not necessarily required for a given term, the specification must, nevertheless, support use of the term. The fact that the claims were amended to replace the recitation of "functional" with "biologically functional" demonstrates that Applicant believes that there is a difference between the terms.

Vas-Cath Inc. v. Mahurkar ((CAFC, 1991) 19 USPQ2d 1111) clearly states that "Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is*

now claimed." (See *Vas-Cath* at page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see *Vas-Cath* at page 1115). See also, the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

7. Claims 1, 2 and 12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

Claim 1 has further been amended to recite a "composition comprising a plurality of complexes...wherein said plurality of complexes are recognizable by a single specific CTL clone." The recited limitation is not supported by the specification or claims as originally filed and constitutes new matter. The specification discloses the making of an MHC class I complex and use of that complex to present specific antigenic peptides to specific CTL clones, for example at page 19, lines 15-17, but the specification does not disclose a "composition" of such complexes that present antigenic peptide to a "single" specific CTL clone. There is no disclosure in the specification of any such composition, nor is there disclosure of an embodiment where multiple complexes are used to present antigen to a single specific CTL clone.

Vas-Cath Inc. v. Mahurkar ((CAFC, 1991) 19 USPQ2d 1111) clearly states that "Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See *Vas-Cath* at page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see *Vas-Cath* at page 1115). See also, the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1, 2, 12 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 2 and 13 are each ambiguous and unclear in the recitation of "biologically functional." The term is not disclosed or defined in the specification, so it is unclear what type of biological functions are exhibited by the complex recited in the claims.

Conclusion

9. No claim is allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571) 272-0852. The examiner can normally be reached on M-Th 6:30-4:00 and Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

F. Pierre VanderVegt, Ph.D.
Patent Examiner
February 21, 2006

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